REMARKS

Claims 1-11 and 13-74 are pending in the present application. Claims 1-11, 13, 27-42 and 63-74 were examined in the Office Action dated June 11, 2008. Claims 14-26 and 43-62 have been withdrawn from consideration after a restriction requirement.

Substance of Interview

A telephonic interview was held on September 19, 2008 between Examiner Regina M. Yoo and Applicants' representatives Michael Harlin, Benjamin Sanders, and Maurie Baker. The interview summary dated September 19, 2008 accurately reflects the substance of the interview, in general, though Applicants' principal arguments are more fully set forth in the following remarks. Applicants request that the Examiner consider and rely upon the following remarks rather than discussion and argument during the September 19th interview.

The Interview Summary stated that the Applicant had pointed out that post-tensioning utilized in the industry (post-sterilization) is by a surgeon immediately prior to implantation to remove slack from the implant. Applicant wishes to clarify that this is a very common application of post-sterilization tensioning, particularly with respect to implants replacing tendons, however there have been other usages of tensioning after sterilization, such as for conditioning an implant, which may be done by an implant manufacturer rather than a surgeon. For example, Cook et al., U.S. 6,206,931 (which has been discussed in previous Office Actions and Responses) states that a "segment of the tela submucosa can be preconditioned for tendon and ligament replacement applications by stretching." (Col. 11, lns. 62-64). Cook `931 also indicates that grafts used in orthopedic applications are typically placed under tension in their surgical installation. (Col. 12, lns. 43-44). Similarly, Abraham et al., U.S. 6,572,650 states that a processed tissue matrix can be subjected to physical modifications such as conditioning by stretching and relaxing. (Col. 3, lns. 18-21). However, such tensioning after sterilization, either by a surgeon or by an implant manufacturer, would not be expected to improve the degree of collagen degradation experienced by the implant, one of the biochemical properties of the implant.

The Interview Summary also noted that Applicants would look into whether data on implants that underwent tensioning prior to sterilization is available to present to the Examiner. Applicants conducted a reasonable inquiry and did not locate studies that compared the tensile strength or collagen degradation of soft tissue implants that underwent tensioning prior to sterilization, but without tensioning during sterilization, to soft tissue implants that were tensioned during sterilization. Applicant is not presently aware of any studies conducted by the Assignee of the present application that make the direct comparison sought by the Examiner, but feel that this data is not necessary as the data in the previously filed declaration and in the instant specification should be sufficient (see discussion below).

Claim Rejections - 35 USC § 102

Claims 27-30, 34-35, 39 and 41 were rejected under 35 U.S.C. 102(e) as being unpatentable over Ogle (20030229394). The Office Action stated that Ogle `394 discloses a process for treating an implant prior to implantation, where crosslinking is disclosed to eliminate antigens and to eliminate hyper-acute immune response. The Office Action asserted that the use of glutaraldehyde also would sterilize the tissue as glutaraldehyde is a known sterilant as well as a fixative/crosslinking agent.

Applicants are amending claim 27 to recite that the sterilant is other than glutaraldehyde. The amendment to claim 27 is supported throughout the specification, for example, at paragraph 04, which indicates that glutaraldehyde is disfavored as a cleaning agent. Ogle does not anticipate claims 27-30, 34-35, 39 and 41 as amended, because it does not disclose contacting a soft tissue with a cleaning agent other than glutaraldehyde while applying tension to the soft tissue. Accordingly, the rejection of those claims should be withdrawn.

Claim Rejections - 35 USC § 103

Claims 38 and 42 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Ogle (2003/0229394) in view of Wolfinbarger (6,024,735). Claims 1-5, 7-11, 13, 27, 31-42, 63-68 and 70-74 were rejected under 35 U.S.C. 103(a) as being unpatentable over Mills (WO 00/29037) in view of Ogle US 20030229394). Claims 6 and 69 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Mills `037 in view of Ogle `394 and further in view of Wolfinbarger `735. Claim 64 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Ogle `394 in view of Wolfinbarger `735.

The Office Action acknowledges that Mills `037 fails to teach that the process for making an implant more suitable for implantation also comprises applying tension or kinematic restraint to the soft tissue at least during part of step (b) or during each of steps (a)-(c). However the Office Action relies on Ogle `394 for its disclosure of applying tension to an implant/soft tissue while the implant is being contacted with glutaraldehyde.

Claims 1-11, 13, 31-33, and 63-74 require contacting an implant comprising a soft tissue with an oxidizing sterilant (such as a peroxide) and applying tension or kinematic restraint to the soft tissue while contacting the soft tissue with oxidizing sterilant. Applicants disclose the following (non-limiting) examples of "oxidizing sterilants": peroxides, oxides, hypochlorites, percarboxylic acids, and ozone. (¶ 062.) Claims 1-11, 13, and 63-74 also require contact with a protective agent selected from the group consisting of alcohols and polyols.

Applicants submit that Ogle `394 is not pertinent to the claimed process. The Ogle reference does not disclose or suggest a process in which an implant comprising a soft tissue is contacted with an oxidizing sterilant (or with a protective agent selected from the group consisting of alcohols and polyols, and an oxidizing sterilant). Ogle `394 is generally unconcerned with processes for cleaning or sterilizing a soft tissue implant. Instead, Ogle `394 is generally concerned with bioprosthetic heart valves and methods of selectively aligning tissue to increase its rigidity so it can be used to form a prosthetic valve. (See Title and Abstract of Ogle `394). In Ogle `394, glutaraldehyde is used as a cross-linking agent. Ogle discloses cross-linking or fixing the tissue in conjunction with

aligning the tissue, not as part of a sterilization process. Moreover, Ogle states that sterilization may be done as "preliminary processing" (¶ 0062), indicating that it is separate from the alignment and fixation of the tissue. Ogle does not disclose the use of an oxidizing sterilant.

Applicants submit that the Ogle reference does not disclose or suggest an oxidizing sterilant, and a person skilled in the art would not have viewed Ogle's teachings about aligning fibrils of a soft tissue implant and fixing the aligned tissue with glutaraldehyde as being relevant to a process of sterilizing an implant comprising a soft tissue by contact with an oxidizing sterilant. Glutaraldehyde is used in Ogle `394 as a cross-linking agent or fixative. Ogle discloses cross-linking or fixing the tissue in conjunction with aligning the tissue, not as part of a sterilization process. Ogle states that sterilization may be done as "preliminary processing" (¶ 0062), indicating that it is separate from the alignment and fixation of the tissue.

Additionally, Ogle teaches away from applying tension to a tendon or ligament suitable for alignment. Applicants' claims 10, 11, 41, 42, 73 and 74 recite that the implant comprises at least one tendon or ligament, or a tendon having bone attached thereto. Although Ogle `394 makes a passing mention of tendons and ligaments as natural tissue materials, the overall teachings of Ogle `394 would have discouraged a skilled person from practicing Ogle's process in making a tendon or ligament implant. Implanted tendons or ligaments should have flexibility in order to function as desired in the body. Ogle teaches that applying tension to increase the rigidity of the tissue. (¶ 0006, 0007, 0060.) While increased rigidity may be desired by Ogle for a heart valve prosthesis (¶ 0045, 0049, 0056), it is generally undesirable for a tendon or ligament implant.

In response to the previous Office Action, Applicants submitted a declaration under Rule 1.132 showing that the claimed process yields **unexpected results**. Applicants established that applying tension to tendons during the sterilization process yielded tendons having improved strength as compared to non-tensioned tendons.

Applicants submitted the Declaration of Arunas A. Zhukauskas ("the Zhukauskas Declaration"), which showed a clinically relevant difference between tendons that were tensioned during sterilized and that were not tensioned during sterilization. "Sterilization" is used here and in the Zhukauskas declaration to refer generally to the claimed process for making an implant more suitable for implantation. The claimed process includes contacting the implant with one or more cleaning agents, such as an oxidizing sterilant. The Zhukauskas declaration showed that tensioning during sterilization yielded tendons having greater ultimate tensile force and ultimate tensile strength. (Zhukauskas Declaration, ¶ 10). This indicates that applying tension to the tendons during the sterilization process yields tendons having improved strength as compared to tendons that were not tensioned during the sterilization process. (Id.)

The Office Action of August 4, 2008 found the Zhukauskas Declaration unpersuasive based on the examiner's belief that the declaration failed to compare samples tensioned during sterilization with samples tensioned separately from sterilization. The Office Action states:

> In addition, Applicant does not provide any data for samples that are tensioned separately from the sterilization process (pre-sterilization and/or post-sterilization) in order to show that simultaneous tensioning and sterilization of the implant material yields unexpected results beyond that expected from tensioning a sample separately from a sterilization step.

(Office Action, page 15). Applicants respectfully submit that the data provided by the Zhukauskas declaration actually reflects the type of comparison desired by the Office Action. The Zhukauskas declaration discloses that all the tendon samples were tensioned after sterilization, as part of the test protocol for determining the tendon strength. (See Zhukauskas declaration, ¶ 8.) As discussed in the declaration, each tendon was subjected to the same test protocol for evaluating tensile strength, which included the application of a pre-defined and automated load profile, culminating in a pull to ultimate failure load for that tendon. (Zhukauskas Declaration, ¶ 8).

More particularly, the load profile of the test protocol included a Tensile Hold phase, in which each of the tendon samples were subjected to a 90-Newton load 3

times, loaded for 60 seconds each time. This Tensile Hold phase of the test protocol is generally intended to simulate the practice of surgeon pre-tensioning in the operating room. Thus both sets of tendons (those tensioned during sterilization, and those not tensioned during sterilization) were tensioned separately from the sterilization process. Accordingly, the test data reported in the Zhukauskas Declaration includes the comparison contemplated by the Office Action; and it shows the effect of tensioning during sterilization compared to tensioning separately from sterilization.

The Office Action acknowledged that the Zhukauskas declaration provides data that appears to indicate that applying tension to the tendons during the sterilization process yields tendons having improved strength as compared to non-tensioned tendons. (Office Action, page 15.) The tendons sterilized without tension failed more easily (with less force applied) than the tendons sterilized under tension. (Id.) Since the data includes a comparison of samples tensioned during (and after) sterilization to samples tensioned only after sterilization, the data should be persuasive and sufficient to establish unexpected results by the claimed process.

The Office Action of August 4, 2008 also did not find the Zhukauskas Declaration persuasive because "it was well known that the step of tensioning implant materials separately from sterilization step yields implants that are stronger than un-tensioned implant material." (Office Action, page 15). Although it may have been known that "the step of tensioning implant materials yields a stronger implant" (Office Action, page 15), it was not known or recognized that tensioning during a sterilization process would prevent a decrease in strength. Tensioning pre- or post-sterilization may align collagen fibrils (as indicated by Ogle). This is a phenomenon which is distinct from the collagen damage which may occur from contact with one or more cleaning agents (particularly an oxidizing sterilant) during sterilization. Applicants have shown that tensioning can reduce collagen damage from contact with chemicals during sterilization. (See Table 1 in the specification.) As a result, tensioning during a sterilization process imparts a benefit over and above tensioning before or after sterilization.

Applicants have already provided evidence of reduced collagen damage. Table 1 in Applicants' specification shows the effects on tendon samples from exposure to various chemicals, including hydrogen peroxide (an oxidizing sterilant) and detergent. The effect of the various chemicals as measured by collagen degradation in the tendon is shown in Table 1, with a higher number indicating more denatured collagen and thus more damage to the tendon. The results in Table 1 show that exposure of the tendon samples to peroxide resulted in denatured collagen in the tendon samples, but when tension was applied to a tendon during the tendon's exposure to the peroxide, there was less collagen degradation.

The Office Action acknowledged that the collagen degradation measured for the non-tensioned implants was higher than for the tensioned implant. However, the Office Action indicated that the collagen degradation results set forth in Table 1 were not persuasive because they are merely "another advantage" which has been recognized by Applicant. Applicants submit that there is no prior art process that applied tension while contacting a soft tissue implant with an oxidizing sterilant. The reduction in collagen degradation found by Applicants is not "another advantage" of a known process, but rather an unexpected benefit of a previously unknown process.

Petition for a One Month Extension of Time

Applicants hereby petition for a one-month extension of time in which to respond to the Office Action of June 11, 2008. The Commissioner is authorized to charge the requisite extension fee of $130.00, and any necessary fees for this submission, to the Deposit Account of McAndrews, Held & Malloy, Account No. 13-0017.

CONCLUSION

For the foregoing reasons, Applicants submit that claims 1-11, 13, 27-42 and 63-74 are in condition for allowance.

The Examiner is invited to telephone Applicants' representative to discuss any questions or if Applicants' representative may be of any assistance to the Examiner in the reconsideration and allowance of this case.

The Commissioner is authorized to charge any necessary fees to the Deposit Account of McAndrews, Held & Malloy, Account No. 13-0017.

Respectfully submitted,

Dated: October 14, 2008

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